

REMARKS

Claims 1, 3, 5-7, 9-10 and 12-14 remain pending in the above-identified application and stand ready for further action on the merits. The present reply is being filed concurrently with a Request for Continued Examination (RCE).

Request for Personal Interview with Examiner

Applicants earnestly request permission to hold a personal interview with Examiner Humera N. Sheikh of the USPTO.

Such an interview request was previously made by the undersigned in a telephone conversation with Examiner Sheikh in October 2005. However, due in part to the prior issuance a final office action on August 2, 2005, Examiner Sheikh indicated that a personal interview could not be granted at that time. Nonetheless, Examiner Sheikh did indicate that an interview could be held at a later date if applicants eventually filed an RCE, thereby changing the after-final status of the case.

Accordingly, Examiner Sheikh is respectfully requested to promptly contact the undersigned (John W. Bailey, Reg. # 32,881) at the below indicated telephone number, to schedule a personal interview at the Examiner's earliest convenience, in order to further expedite prosecution of this case to allowance, if the present reply does not result in an allowance of each of the pending claims.

Claim Rejections Under 35 USC § 103

Claims 1, 3, 5-7, 9-10 and 12-14 are rejected under 35 USC § 103(a) as being unpatentable over Pierre et al. US '318 (US 5,300,318). Claims 1, 3, 5-7, 9-10 and 12-14 have also been rejected under 35 USC § 103(a) as being unpatentable over Koyama et al. US '914 (US 5,855,914). Reconsideration and withdrawal of each of these rejections is respectfully requested based upon the following remarks.

Legal Standard for Determining Obviousness

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

"There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." In re Rouffet, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998) (The combination of the references taught every element of the claimed invention, however

without a motivation to combine, a rejection based on a *prima facie* case of obvious was held improper.). The level of skill in the art cannot be relied upon to provide the suggestion to combine references. Al-Site Corp. v. VSI Int'l Inc., 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999).

"In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification." In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972).

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." In re Kotzab, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). See also In re Lee, 277 F.3d 1338, 1342-44, 61 USPQ2d 1430, 1433-34 (Fed. Cir. 2002) (discussing the importance of relying on objective evidence and making specific factual findings with respect to the motivation to combine references); In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Previously Submitted 37 CFR § 1.132 Declarations

The Applicants have previously submitted three separate 37 CFR § 1.132 declarations to show the superiority of the present invention. The Examiner is respectfully requested to review and reconsider the evidence contained in these earlier submitted declarations at this time. The previously submitted 37 CFR S 1.132 Declarations are as follows.

Declaration Number	Declarant (Date of Signing)	Date filed in USPTO
First	Yasushi Ochiai (November 11, 2003)	November 18, 2003
Second	Yasushi Ochiai (June 23, 2004)	June 24, 2004
Third	Yasushi Ochiai (June 1, 2005)	June 6, 2005

In the First and Second Ochiai 37 CFR § 1.132 declarations, comparative testing between Pierre et al. and the present invention is set forth. Pierre et al. only specifically disclose the manufacturing method in the working example. However, the USPTO Examiner, nonetheless requested comparative testing even in view of such a mere description. In this respect, it is considered an undue burden for the USPTO to continue any request that Applicant carry out a further comparison with Pierre et al., as there is no definitive way to know how to obtain a granule based on the mere description that is provided in the cited Pierre et al. working example.

In the Third Ochiai 37 CFR § 1.132 declaration, the importance of granular strength is shown. In this respect, the experiment is *not* intended to show the superiority of the claimed invention *per se*, since the Applicant has already shown the importance of a granular strength of 650 gf/mm that the Examiner has requested. Instead, the Experiment is provided to show that the granular strength of the present inventive granules is quite distinct and different from that of Koyama et al. US '914.

Present Invention and Its Advantages

The present invention relates to a method of manufacturing drug granules, and more particularly provides a pharmaceutical preparation containing a water-soluble drug as an active ingredient at a high density, which shows superior stability in a uniform content.

In the method of manufacturing a drug granule as instantly recited in claim 1, a granulation step occurs “of spraying only a solution of a water soluble drug on a crystal of said water soluble drug substantially without using a binder or in the absence of binder in a rotary fluidized bed granulate coating apparatus, wherein the drug granule has a granular strength of 650-2500 gf/mm².” (See claim 1, *emphasis added*.)

An important aspect of the present invention relates to the granular strength of the granules, since it allows for the granules to be “tableted” or subjected to a “tableting” step, without breaking of the granules. This aspect of the present invention is also significant when the claimed inventive methods also contain a step of “coating said drug granule with a release control film coating agent.” (See claims 7, 9-10 and 14.)

Distinctions Over the Cited Art

The above aspects of the present invention are nowhere taught, disclosed or otherwise rendered obvious by the disclosure of Pierre et al. US '318 or Koyama et al. US '914.

Pierre et al. US '318

For example, Pierre et al. (US '318) does not provide any suggestion regarding granular strength and/or tableting of coated granules. In contrast to the teachings of Pierre et al. US '318, the present invention provides granules having sufficient granule strength to be capable of maintaining a coating film during tableting processes, and thereby also allow for the manufacture of tablets from the coated granules having desirable and suitable dissolution characteristics. On this point, the Examiner is again invited to review Mr. Ochiai's earlier filed *First* and *Second* 37 CFR § 1.132 declarations (filed with the USPTO on November 18, 2003 and June 24, 2004, respectively).

The method of claim 1 can also be distinguished from Pierre et al. US '318, since a "rotary fluidized bed granulate coating apparatus" is used by present inventors, which is different from the type of granulator taught by Pierre et al. US '318, and produces non-expected results when compared with Pierre et al. US '318. More particularly, unlike instant claim 1, which recites the use of a *rotary* fluidized bed granulator, Pierre uses an Uniglatt apparatus (which is a *non-rotary* fluidized bed coating device).

Further, there is provided no teaching or any information in the cited Pierre et al. US '318 reference that would lead one to the unexpected results that are associated with the present

invention. Which unexpected results are, namely, that a difference in *resistance ability to acid solution* is achieved with the present invention that is not envisioned, obtained or otherwise rendered obvious by the teachings and disclosure of Pierre et al. US '318.

Still further, even if one skilled in the art were to assume that generally speaking, the density of a granulate from a *rotary* fluidized bed granulator is much higher than that obtained from a fluidized bed coating device; nonetheless, in the cited Pierre et al. US '318 reference, there is provided no information about granular strength and/or properties of coated granules, and importantly, there are not obtained the advantageous results that are associated with the instant invention as claimed.

Koyama et al. US '914

As also evidenced in the previously submitted *Third* declaration of Mr. Ochiai (filed with the USPTO on June 6, 2005), test results provided show that the granular strength of the present inventive granules is quite distinct and different from that of Koyama et al. US '914.

Further to the above, Mr. Ochiai clearly states in his *Third* declaration that "The granules of prior arts do not have enough strength for tableting without substantial amount of binder. On the other hand the granules of present invention does not need substantial amount of binder to have enough strength for tableting." Mr. Ochiai further states "I believe that prior arts do not teach nor suggest the granule or method of manufacturing granule of present invention comprising a granulation step of spraying only a solution of a water soluble drug on a crystal of said water soluble drug substantially without using a binder or in the absence of binder in a

rotary fluidized bed granulate coating apparatus, wherein the drug granule has a granular strength of 650-2500 gf/mm².”

Accordingly, based upon a consideration of the above remarks and the test results reported in Mr. Ochiai's earlier submitted *Third* 37 CFR § 1.132 declaration, it follows that the outstanding rejection under 35 USC § 103(a) of claims 1, 3, 5-7, 9-10 and 12-14 under 35 USC § 103(a) as being unpatentable over Pierre et al. US '318 or Koyama et al. US '914 must now be withdrawn.

CONCLUSION

Based upon the remarks presented herein, as well as the comparative testing results and conclusions based thereon set forth in Mr. Ochiai's three earlier submitted 37 CFR § 1.132 declarations, the Examiner is respectfully requested to issue a Notice of Allowance clearly indicating that each of the pending claims 1, 3, 5-7, 9-10 and 12-14 are allowable at present.

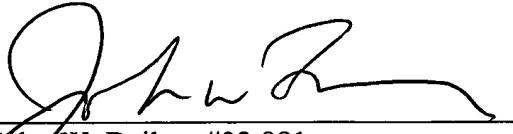
Likewise, should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact John W. Bailey (Reg. No. 32,881) at the telephone number below, to schedule and conduct an interview in an effort to expedite prosecution in connection with the present application.

Docket No. 4367-0101P
Appl. No. 10/091,559

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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By 
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